ADMINISTRATIVE ORDER
No. 2018- 0013

SUBJECT: Revised Guidelines on the Management of Rabies Exposures

I. BACKGROUND AND RATIONALE

Rabies is a fatal disease in developing countries where animal immunization and control of dogs are inadequate. In view of the 100% case fatality of human rabies, the prevention of rabies infection after exposure is of utmost importance.

The Department of Health (DOH), having committed itself to the prevention of human deaths due to rabies, provides vaccines to high-risk exposed patients for Post-Exposure Prophylaxis (PEP) through the Animal Bite Treatment Centers (ABTCs). In 1997, the National Rabies Prevention and Control Program introduced the intradermal (ID) administration of rabies cell culture and embryonated egg-based vaccines (CCEEV), an economical regimen that reduces the cost of PEP by as much as 60-80%. The DOH maintains the use of the intradermal regimen for PEP at the ABTCs. The DOH procures human anti-rabies vaccines which are registered by the Philippine Food and Drug Administration (FDA), listed in the Philippine National Drug Formulary and pre-qualified by the World Health Organization (WHO).

Over the past two years, the number of animal bite victims seeking PEP has increased to over 1 Million cases per year. While the demand for human rabies vaccine is increasing in the country, there is an anticipated global shortage of the said vaccine due to issues in the production of one WHO prequalified vaccine.

Of recent, WHO provided recommendations on shorter and more feasible protocols for PEP and Pre-Exposure Prophylaxis (PrEP).

This AO is to update the guidelines on PEP and PrEP and to provide guidance on the selection and use of human rabies vaccine to help address the global shortage of WHO pre-qualified human rabies vaccines.

All government health workers at all levels shall adopt these treatment guidelines to ensure standard and rational management of rabies exposures. Private practitioners in the country are strongly encouraged to adopt these treatment guidelines.
II. OBJECTIVE

To update policy guidelines and procedures on provision of PEP and PrEP to address the global shortage of human rabies vaccine and immunoglobulins.

III. COVERAGE

All government health workers at all levels shall adopt these treatment guidelines to ensure standard and rational management of rabies exposures. Private practitioners in the country are strongly encouraged to adopt these treatment guidelines.

IV. DEFINITION OF TERMS

A. Active Immunization – refers to the administration of a vaccine to induce protective immune response.

B. Cell Culture & Embryonated Egg –based Vaccine (CCEEV) - vaccines that use mammalian cell lines (cell-culture) as well as embryonated eggs in the isolation, titration of animal viruses and cultivation to produce vaccines. CCEEV include Purified Vero Cell Rabies Vaccine (PVRV), Human Diploid Cell Vaccine (HDCV) and Purified Chick Embryo Vaccine (PCEV). CCEEV will replace everything that refers to Tissue Culture Vaccine (TCV).

C. Immunocompromised host – refers to patients receiving immunosuppressive drugs such as systemic steroids (not topical or inhaled) and chemotherapeutic drugs for cancer, AIDS and HIV infected patients and patients with immune deficiency. These patients are expected to have lower immune response to immunization.

D. Incubation Period – refers to the period from the time of exposure up to the appearance of first clinical symptoms of rabies. It is extremely variable ranging from 4 days to 7 years; but generally 20 to 90 days.

E. Observation Period – refers to animal observation for 14 days from the time of bite until the appearance of expected symptoms of rabies.

F. Passive Immunization – refers to the administration of pre-formed antibodies (immune globulins or passive immunization products) to provide immediate protection. These antibodies come from either human or animal source.

G. Post-Exposure Prophylaxis (PEP) – formerly post exposure treatment (PET); refers to anti-rabies treatment administered after an exposure (such as bite, scratch, lick, etc.) to potentially rabid animals. It includes local wound care, administration of rabies vaccine with or without Rabies Immune Globulin (RIG) depending on category of exposure.

H. Pre-exposure prophylaxis (PrEP) – refers to rabies vaccination administered before an exposure to potentially rabid animals. This is usually given to those who are at high risk of getting rabies such as veterinarians, animal handlers, staff in the rabies laboratory, hospitals handling rabies patients and school children from high risk areas, etc.
I. Prodromal Period – refers to the period lasting for 10 days with non-specific manifestations, which include fever, sore throat, anorexia, nausea, vomiting, generalized body malaise, headache and abdominal pain. Paresthesia or pain at the site of the bite is due to viral multiplication at the spinal ganglion just before it enters the brain.

J. Rabid Animal – refers to biting animal with clinical manifestation of rabies and/or confirmed laboratory findings.

K. Suspected Rabid Animal – refers to biting animal with a potential to have rabies infection based on unusual behavior, living condition like stray dogs, endemicity of rabies in the area and no history of immunization.

L. Rabies Immunoglobulin (RIG) - is an injectable preparation of rabies antibody administered to unvaccinated persons to provide immediate but temporary protection until the body can actively produce antibodies of its own induced by the human rabies vaccine.

M. Vaccine Potency – refers to the amount of acceptable active ingredients in a rabies vaccine which is expected to provide at least minimum protection.

V. GENERAL GUIDELINES

A. Management of animal bite cases, including provision of human rabies vaccine, is a joint responsibility of the Department of Health and the Local Government Units.

B. Rabies Control Program shall be integrated to the regular health services provided by local health facilities of bite victims, as a measure.

C. PEP and PrEP shall be carried out by Local Government Units through the Animal Bite Treatment Centers with the technical and logistical assistance from the Department of Health.

D. Funding requirements needed for management of rabies exposures and pre-exposure prophylaxis and for operational systems shall be planned, secured and allotted for by the implementing agencies, particularly, the Department of Health and the Local Government Units.

E. Advocacy through information dissemination and training of health workers shall be conducted at all levels.

F. Collaboration and coordination among government agencies, non-government and private organizations to ensure successful implementation shall be strengthened.

VI. SPECIFIC GUIDELINES AND PROCEDURE

A. Management of Potential Rabies Exposure

1. Initiation of post-exposure prophylaxis (PEP) shall not be delayed for any reason regardless of interval between exposure and consultation as it increases the risk of rabies and it is associated with treatment failure.

2. Immediate washing of the bite wound/ exposed area with soap and water and application of an antiseptic solution reduces the risk of rabies transmission.

3. There are no absolute contraindications to rabies PEP. Patients allergic to a specific vaccine/RIG or its components shall be given the alternative vaccine/RIG.
4. Table shows the categories of exposure to a rabid animal or to an animal suspected to be rabid, with their corresponding management guidelines:

Table 1. Categories of Rabies Exposure with Corresponding Management

<table>
<thead>
<tr>
<th>Category of exposure</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>CATEGORY I</td>
<td></td>
</tr>
<tr>
<td>a) Feeding/touching an animal</td>
<td>1. Wash exposed skin immediately with soap and water.</td>
</tr>
<tr>
<td>b) Licking of intact skin (with reliable history and thorough physical examination)</td>
<td>2. No vaccine or RIG needed</td>
</tr>
<tr>
<td>c) Exposure to patient with signs and symptoms of rabies by sharing of eating or</td>
<td>3. Pre-exposure prophylaxis may be considered for high risk persons.</td>
</tr>
<tr>
<td>drinking utensils</td>
<td></td>
</tr>
<tr>
<td>d) Casual contact (talking to, visiting and feeding suspected rabies cases) and</td>
<td></td>
</tr>
<tr>
<td>routine delivery of health care to patient with signs and symptoms of rabies</td>
<td></td>
</tr>
<tr>
<td>CATEGORY II</td>
<td></td>
</tr>
<tr>
<td>a) Nibbling of uncovered skin with or without bruising/hematoma</td>
<td>1. Wash wound with soap and water.</td>
</tr>
<tr>
<td>b) Minor/superficial scratches/abrasions without bleeding, including those induced</td>
<td>2. Start vaccine immediately.</td>
</tr>
<tr>
<td>to bleed</td>
<td></td>
</tr>
<tr>
<td>c) All Category II exposures on the head and neck area are considered Category III</td>
<td>3. Complete vaccination regimen until Day 7 regardless of the status of the</td>
</tr>
<tr>
<td>and shall be managed as such.</td>
<td>biting animal</td>
</tr>
<tr>
<td></td>
<td>4. RIG is not indicated</td>
</tr>
</tbody>
</table>
### CATEGORY III

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>Transdermal bites (puncture wounds, lacerations, avulsions) or scratches/abrasions with spontaneous bleeding</td>
</tr>
<tr>
<td>b)</td>
<td>Licks on broken skin or mucous membrane</td>
</tr>
<tr>
<td>c)</td>
<td>Exposure to a rabies patient through bites, contamination of mucous membranes (eyes, oral/nasal mucosa, genital/anal mucous membrane) or open skin lesions with body fluids through splattering and mouth-to-mouth resuscitation.</td>
</tr>
<tr>
<td>d)</td>
<td>Unprotected handling of infected carcass</td>
</tr>
<tr>
<td>e)</td>
<td>Ingestion of raw infected meat</td>
</tr>
<tr>
<td>f)</td>
<td>Exposure to bats</td>
</tr>
<tr>
<td>g)</td>
<td>All Category II exposures on head and neck area</td>
</tr>
</tbody>
</table>

1. Wash wound with soap and water.
2. Start the vaccine and RIG immediately.
3. Complete vaccination regimen until Day 7 regardless of the status of the biting Animal.

10. Dog owners have the responsibility to keep their dogs for observation under the Rabies Act of 2007, with penalties to violators provided for by the law.
11. Only the Intradermal Regimen will be used in the administration of vaccine in all government facilities except for conditions that require IM administration as described in Section C.1.d Post-Exposure Prophylaxis under Special Conditions.

### B. Immunization

1. Active Immunization

   a. Administration
   
   Vaccine shall be administered to induce antibody and T-cell production in order to neutralize the rabies virus in the body. It induces an active immune response in 7-10 days after vaccination, which may persist for years provided that primary immunization is completed.

   b. Types of Rabies Vaccines and Dosage
   
   The National Rabies Prevention and Control Program (NRPCP) shall provide the following CCEEV a) Purified Vero Cell Rabies Vaccine (PVRV) – 0.5 ml/vial and b) Purified Chick Embryo Cell Vaccine (PCECV) - 1.0 ml/vial. (Table 2)
Table 2. List of CCEEV provided by the NRPCP to Animal Bite Treatment Centers with Corresponding Preparation and Dose

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Preparation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purified Verocell Rabies Vaccine (PVRV)</td>
<td>0.5 ml/vial</td>
<td>ID - 0.1 ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IM - 0.5 ml</td>
</tr>
<tr>
<td>Purified Chick Embryo Cell Vaccine (PCECV)</td>
<td>1 ml/vial</td>
<td>ID - 0.1 ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IM - 1.0 ml</td>
</tr>
</tbody>
</table>

c. Recommendations on the intradermal administration of anti-rabies vaccines:

The NRPCP introduced the intradermal (ID) use of rabies tissue culture vaccines in the country in 1997. The Philippines was among the first countries to adopt this regimen as recommended by the World Health Organization, in order to totally discontinue the use of nerve tissue vaccine (NTV) which was associated with vaccine induced encephalopathy. To mitigate the expected increase in the cost of PEP with the shift from NTV to CCEEV, the ID use of these vaccines was introduced. According to WHO, the ID use of CCEEV can decrease the cost of PEP by as much as 60-80%.

However, only a limited number of commercially available rabies vaccines have been proven, to date, as safe and efficacious for PEP when administered by the ID route. Recently, local manufacturers in rabies-endemic countries have started to produce rabies vaccines. The ID use of these vaccines shall be based on adherence to WHO requirements for that route and approval by national health authorities as follows, “New vaccine manufacturers should provide clinical evidence that their products are immunogenic and safe when used intradermally. Clinical evidence should include clinical trials involving a vaccine of known immunogenicity and efficacy when used by this route as control, serological testing with rapid fluorescent focus inhibition test, and publication in internationally peer-reviewed journals”.

To ensure compliance to these recommendations and guarantee that animal bite patients seeking treatment in government Animal Bite Treatment Centers receive only CCEEVs that have been proven to be safe and effective, the program shall utilize for its intradermal regimen only CCEEVs that satisfy the following criteria:

c.1. The vaccine is WHO prequalified (http://www.who.int/immunization_standards/vaccine_quality/ PQ_vaccine_list_en/en/index.html) and registered and approved by FDA;

c.2 For vaccines that are non-prequalified, the vaccine shall be registered with and approved by the Food and Drug Administration;

c.3. The vaccine must have gone through clinical trials on safety, immunogenicity and efficacy in comparison with a vaccine of demonstrated efficacy which are published in peer reviewed trials;
c.4 The potency of vaccines for ID use shall be at least 0.5 IU/ID dose as evidenced by their lot release certificate. The potency of the vaccine batch shall be provided by the manufacturer;
c.5 The product insert shall contain the vaccine’s approved ID dose and consistent with its Certificate of Registration (CPR); and
c.6. Non-WHO prequalified vaccines may be used only during shortage of WHO prequalified vaccines. The same criteria shall apply except for c.1.

2. Passive Immunization

Rabies immunoglobulin or RIG (also called passive immunization products) shall be given in combination with rabies vaccine to provide the immediate availability of neutralizing antibodies at the site of the exposure before it is physiologically possible for the patient to begin producing his or her own antibodies after vaccination. This is especially important for patients with Category III exposures. RIGs have a half-life of approximately 21 days.

a. Types of Rabies RIG

a.1. Human Rabies Immune Globulin (HRIG) derived from plasma of human donors administered at a maximum of 20 IU per kilogram body weight. Available preparation is 2 ml/vial; 150 IU/ml

a.2. Highly purified antibody antigen binding fragments [F(ab’)2] produced from equine rabies immune globulin (ERIG) administered at a maximum of 40 IU per kilogram body weight. Available preparation is 5 ml/vial; 200 IU/ml

a.3. Equine Rabies Immunoglobulin (ERIG) derived from purified horse serum administered at 40 IU per kilogram body weight. Available preparation is 5 ml/vial; 200 IU/ml

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Preparation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Rabies Immune Globulin (HRIG)</td>
<td>150 IU/ml at 2 ml/vial</td>
<td>20 IU/kg</td>
</tr>
<tr>
<td>Equine Rabies Immune Globulin (ERIG, a.2 or a.3)</td>
<td>200 IU/ml at 5 ml/vial</td>
<td>40 IU/kg</td>
</tr>
</tbody>
</table>

Table 3. List of Rabies Immunoglobulins provided by the NRPCP to Animal Bite Treatment Centers
b. Rabies Immunoglobulin Criteria:
   To ensure that only safe and efficacious RIG are provided by the National Rabies Prevention and Control Program to all ABTCs, the program shall be guided by the following criteria in procuring the RIG:

   b.1 RIG must be registered and approved by FDA;
   b.2 RIG must be proven to be safe and effective when used together with human rabies vaccine as evidenced by publication on peer-reviewed journals. These include studies on:
   - Safety;
   - Efficacy;
   - Immunogenicity on non-interference when used with anti-rabies vaccine;
   - Animal survivorship, if any; and
   - Post-marketing surveillance

   b.2.3. Results of RFFIT showing antibody content as claimed by the manufacturer

c. Who should be prioritized to be given RIG
   c.1. Even if RIG is not available or affordable, prompt local treatment of all bite wounds or scratches, and for category II and III exposures a complete course of rabies vaccine is indicated.
   c.2. For patients who can reliably document previous post-exposure prophylaxis (PEP of 6 doses (3 visits) or PrEP of 4 doses (2 visits) using WHO pre-qualified CCEEV or PEP of 8 doses (4 visits) or PrEP of 6 doses (3 visits) using non-WHO pre-qualified CCEEV, RIG is not indicated.
   c.3. In cases of shortage or unaffordability, the following groups should be prioritized for RIG allocation:
   - Multiple bites
   - Deep wounds
   - Highly innervated parts of the body, as head, neck, hands, genitals
   - Immunocompromised patients
   - History of biting animal indicative of confirmed or probable* rabies
   - A bite or scratch or exposure of a mucous membrane by a bat can be ascertained

d.3 Computation and Dosage of Rabies Immune Globulin
   - HRIG at 20 IU/kg, body weight (150 IU/ml)
     50 kg. patient x 20 IU/kg. = 1000 IU
     1000 IU ÷ 150 IU/ml = 6.7 ml.

   - ERIG/ F(ab')2 at 40 IU/kg, body weight (200 IU/ml)
     50 kg. patient x 40 IU/kg. = 2000 IU
     2000 IU ÷ 200 IU/ml = 10 ml.
c.4 Administration

c.4.1. The total computed RIG shall be infiltrated around and into the wound as much as anatomically feasible, even if the lesion has healed. In case some amount of the total computed dose of RIG is left after all wounds have been infiltrated, the remaining volume of RIG that is not infiltrated into the wound does not need to be injected IM. It may be reserved for the next patient who needs RIG, ensuring aseptic retention of the RIG i.e. fractionated in smaller individual syringes.

c.4.2. A gauge 23 or 24 needle, 1 inch length shall be used for infiltration. Multiple needle injections into the same wound shall be avoided.

c.4.3 Equine immunoglobulins (ERIG) are clinically equivalent to human rabies immunoglobulins (HRIG) and are considered safe and efficacious life- and cost-saving biologics. Skin testing for ERIG is highly recommended.

c.4.4 If a finger or toe needs to be infiltrated, care shall be taken to ensure that blood circulation is not impaired. Injection of an excessive amount may lead to cyanosis, swelling and pain.

c.4.5 RIG shall not exceed the computed dose as it may reduce the efficacy of the vaccine. If the computed dose is insufficient to infiltrate all bite wounds, it may be diluted with sterile saline 2 or 3-fold for thorough infiltration of all wounds.

c.4.6. RIG shall always be given in combination with rabies vaccine. RIG shall be administered at the same time as the first dose of rabies vaccine (Day 0). In case RIG is unavailable on DAY 0, it may still be given until 7 days after the first dose of the vaccine. Beyond Day 7, regardless of whether day 3 and day 7 doses were received, RIG is not indicated because an active antibody response to the rabies CCEEV has already started and interference between active and passive immunization may occur.

c.4.7. In the event that RIG and vaccine cannot be given on the same day, the vaccine shall be given before RIG because the latter inhibits the level of neutralizing antibodies induced by immunization.

c.4.8. RIG shall be given only once during the same course of PEP.

c.4.9 All bite centers shall be equipped to handle allergic reactions, should they occur.

c.4.10. Patient shall be observed for at least one hour after injection of ERIG for immediate allergic reactions.

c.4.11 Severe adverse events or perceived lower efficacy of RIG (e.g. batches of insufficient potency or lower purification degree) should be monitored, recorded and reported, so that biological producers receive immediate feedback and can respond accordingly. A classification of adverse events is available in Table 6. Post-marketing surveillance is recommended.
c.5 Management of Adverse Reactions
Adverse reactions shall be managed as follows:

c.5.1 Anaphylaxis
- Give 0.1% adrenaline or epinephrine (1:1,000 or 1mg/ml) underneath the skin or into the muscle.
  Adults - 0.5 ml
  Children - 0.01ml/kg, maximum of 0.5 ml
- Repeat epinephrine dose every 10-20 minutes for 3 doses
- Give steroids after epinephrine

c.5.2 Hypersensitivity reactions
- Give antihistamines, either as single drug or in combination
- If status quo for 48 hrs despite combination of antihistamines, may give short course (5-7 days) of combined oral antihistamines plus steroids
- If patient worsens and condition requires hospitalization or becomes life threatening, may give IV steroids in addition to antihistamines

C. Treatment
1. Post- Exposure Prophylaxis

a. Local Wound Treatment
a.1.1. Wounds shall be immediately and vigorously washed and flushed with soap or detergent, and water preferably for 10 minutes. If soap is not available, the wound shall be thoroughly and extensively washed with water.

a.1.2. Apply alcohol, povidone iodine or any antiseptic.

a.1.3. Suturing of wounds shall be avoided at all times since it may inoculate virus deeper into the wounds. Wounds may be coapted using sterile adhesive strips. If suturing is unavoidable, it should be delayed for at least 2 hours after administration of RIG to allow diffusion of the antibody to occur through the tissues.

a.1.4. Any ointment, cream or wound dressing shall not be applied to the bite site because it will favor the growth of bacteria and will occlude drainage of the wound, if any

a.1.5. Anti-tetanus immunization may be given, if indicated. History of tetanus immunization (TT/DPT/Td) should be reviewed. Animal bites shall be considered tetanus prone wounds. Completion of the primary series of tetanus immunization is recommended.
Table 4. Guide to Tetanus Prophylaxis in Routine Wound Management

<table>
<thead>
<tr>
<th>Indication for TT Immunization</th>
<th>Vaccination History</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unknown or &lt;3 Doses</td>
</tr>
<tr>
<td>Td*</td>
<td>TIG/ATS</td>
</tr>
<tr>
<td>All Animal Bites</td>
<td>YES</td>
</tr>
</tbody>
</table>

*Tdap may be substituted for Td if the person has not received Tdap and is 10 years or older; DPT may be given for patients < 7 years old; TT may be given if Td not available
**Yes, if more than 5 years since last dose

b. Routine Wound Management

b.1. The most common organism isolated from dog and cat bites is *Pasteurella multocida*. Other organisms include *S. aureus, Bacteroides sp, Fusobacterium* and *Capnocytophaga*. Antimicrobials shall be recommended for the following conditions:

b.1.1. All frankly infected wounds
b.1.2. All category III cat bites
b.1.3. All other category III bites that are either deep, penetrating, multiple or extensive or located on the hand/face/genital area

b.2. Recommended antimicrobials for frankly infected wounds include:

b.2.1. Amoxicillin/clavulanic

- Adults - 500 mg p.o. TID
- Children - 30-45 mg/kg/day in 3 divided doses

b.2.2. Cloxacillin

- Adults - 500 mg p.o. QID
- Children - 10-150-100 mg/kg/day in 4 divided doses

b.2.3. Cefuroxime axetil

- Adults - 500 mg p.o. BID
- Children - 10-15 mg/kg/day in 2 divided doses

b.2.4. For penicillin allergic patients

- Adults - Doxycycline
- Children – Erythromycin

b.2.5. For those instances where there are no obvious signs of infection, amoxicillin as prophylaxis may suffice

- Adults - 500 mg p.o. TID
- Children - 30-45 mg/kg/day in 3 divided doses

- The public shall be educated in simple local wound treatment and warned not to use procedures that may further contaminate the wounds (e.g. tandok, bato, rubbing garlic on the wounds and other non-traditional practices)
c. Vaccination

c.1. General Principles
   c.1.1. Storage
      c.1.1.1. Vaccines shall be stored at +2 to +8 °C in a refrigerator, not freezer
      c.1.1.2. Once reconstituted, vaccines shall be kept in the refrigerator and used
              within 8 hours
   c.1.2. Administration Area
      c.1.2.1. Injections shall be given on the deltoid area of each arm in adults or at
              the anterolateral aspect of the thigh in infants.
      c.1.2.2. Vaccine shall never be injected in the gluteal area as absorption is
              unpredictable

c.2. Treatment Regimen Schedule
   c.2.1. Updated 2-Site Intradermal Schedule (2-2-2-0-2)
      c.2.1.1. One dose for ID administration is equivalent to 0.1 ml for
              PVRV and PCECV
      c.2.1.2. One dose shall be given on each deltoid on Days 0, 3, 7 and 28
      c.2.1.3. One intradermal dose should have at least 0.5 IU vaccine
              potency

Table 5. Updated 2-Site Intradermal Schedule

<table>
<thead>
<tr>
<th>Day of immunization</th>
<th>PVRV/ PCEV</th>
<th>Site of injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0.1 ml</td>
<td>Left and right deltoids or anterolateral thighs in infants</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.1 ml</td>
<td>Left and right deltoids or anterolateral thighs in infants</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.1 ml</td>
<td>Left and right deltoids or anterolateral thighs in infants</td>
</tr>
<tr>
<td>Day 28*</td>
<td>0.1 ml</td>
<td>Left and right deltoid or anterolateral thighs in infants</td>
</tr>
</tbody>
</table>

* For WHO pre-qualified vaccines, the day 28 dose may be omitted following the IPC Institute Pasteur du Cambodge (IPC) Intradermal regimen (2-2-2-0-0)

Table 6. IPC Institute Pasteur du Cambodge (IPC) Intradermal regimen (2-2-2-0-0)

<table>
<thead>
<tr>
<th>Day of immunization</th>
<th>PVRV/ PCEV</th>
<th>Site of injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0.1 ml</td>
<td>Left and right deltoids or anterolateral thighs in infants</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.1 ml</td>
<td>Left and right deltoids or anterolateral thighs in infants</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.1 ml</td>
<td>Left and right deltoids or anterolateral thighs in infants</td>
</tr>
</tbody>
</table>
c.2.1.4. The ID injection shall produce a minimum of 3 mm wheal. In the event that a dose of vaccine is inadvertently given subcutaneously or IM, the dose shall be repeated.

c.2.1.5. A one (1) ml syringe with gauge 27 needle, preferably auto-disposable syringe, shall be used for ID injection.

c.2.1.6. Should a vaccine dose be delayed for any reason, the PEP regimen should be continued (not restarted).

c.2.3. Intramuscular Regimens approved by WHO

c.2.3.1. Zagreb Regimen Schedule (2-0-1-0-1) Intramuscular Schedule

<table>
<thead>
<tr>
<th>Day of immunization</th>
<th>PVRV</th>
<th>PCECV</th>
<th>Site of injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>Left and right deltoïds or anterolateral thigh in infants</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>One deltoïd or anterolateral thigh in infants</td>
</tr>
<tr>
<td>Day 21</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>One deltoïd or anterolateral thigh in infants</td>
</tr>
</tbody>
</table>

Table 7. Zagreb Regimen Schedule (2-0-1-0-1) Intramuscular Schedule

c.2.3.2. Shortened Intramuscular Schedule (CDC) (1-1-1-1-0)

<table>
<thead>
<tr>
<th>Day of immunization</th>
<th>PVRV</th>
<th>PCECV</th>
<th>Site of injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>One deltoïd or anterolateral thigh in infants</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>One deltoïd or anterolateral thigh in infants</td>
</tr>
<tr>
<td>Day 7</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>One deltoïd or anterolateral thigh in infants</td>
</tr>
<tr>
<td>Day 14</td>
<td>0.5 ml</td>
<td>1.0 ml</td>
<td>One deltoïd or anterolateral thigh in infants</td>
</tr>
</tbody>
</table>

Table 8. Shortened Intramuscular Schedule (CDC) (1-1-1-1-0)

d. Post-Exposure Prophylaxis under Special Conditions

d.1. Pregnancy and infancy shall NOT be contraindications to treatment with purified CCEEV (PVRV, PCECV) and RIG.

d.2. Babies who are born of rabid mothers shall be given rabies vaccination as well as RIG as early as possible at birth.
d.3. Patients with hematologic conditions where IM injection is contraindicated shall receive rabies vaccine by ID route.

d.4. Patients with chronic liver disease and those taking chloroquine, and systemic steroids shall be given standard IM regimen as the response to ID regimen is not optimum for these conditions. Vaccination shall not be delayed in these circumstances as it increases the risk of rabies.

d.5. Immunocompromised individuals (such as those with HIV infection, cancer/transplant patients, patients on immunosuppressive therapy etc.) shall be given vaccine using standard IM regimen and RIG for both Category II and III exposures.

d.6. Exposed persons who present for evaluation or treatment weeks or months after the bite shall be treated as if exposure has occurred recently. However, if the biting animal has remained healthy and alive with no signs of rabies until 14 days after the bite, no treatment shall be needed.

d.7. Changes in the human rabies vaccine product and/or the route during the same PEP course are acceptable, if unavoidable to ensure PEP course completion. Restarting PEP is not necessary.

d.8. Bites by rodents, guinea pigs and rabbits shall not require rabies post-exposure prophylaxis.

d.9. Bites by domestic animals (dog, cat) and livestock (cows, pigs, horses, goats etc) as well as wild animals (bats, monkeys, etc) shall require PEP.

**e. Post-Exposure Prophylaxis of Previously Immunized Animal Bite Patients**

e.1. Local wound treatment shall always be carried out.

e.2. Persons with repeat exposure after having previously received complete primary immunization or Pre-Exposure Prophylaxis against rabies with CCEEV shall be given a booster dose of 0.1 ml ID dose at 1 site on D0 and D3 or 4 ID doses on Day 0. To maximize use of CCEEV, the use of an IM booster dose is discouraged.

**Table 9a. Management of Previously Vaccinated Individuals**

<table>
<thead>
<tr>
<th>PEP/PrEP History</th>
<th>RIG</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient received complete PrEP (Day 0 and 7) OR Patient received at least days 0 and 3 doses of PEP ID/IM</td>
<td>No</td>
<td>Determine if high or low risk bite (see Table 9b)</td>
</tr>
<tr>
<td>Patient received complete PrEP (Day 0 and 7) OR Patient received at least days 0 and 3 doses of PEP ID/IM AND Patient is immunocompromised OR bitten by a bat</td>
<td>Yes, if indicated</td>
<td>Give full course PEP</td>
</tr>
<tr>
<td>Patient did not complete PrEP OR Patient received only 1 dose of PEP</td>
<td>Yes, if indicated</td>
<td>Give full course PEP</td>
</tr>
</tbody>
</table>
Table 9b. Criteria for high and low risk exposures

<table>
<thead>
<tr>
<th>Risk exposure</th>
<th>Criteria</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk</td>
<td><strong>ANY ONE OF THE FOLLOWING:</strong></td>
<td>Immediately provide the booster injections to the patient</td>
</tr>
<tr>
<td></td>
<td>1. Biting animal cannot be observed, dies or is sick</td>
<td><strong>Booster doses:</strong></td>
</tr>
<tr>
<td></td>
<td>2. Site of bite is in highly innervated parts of the body – neck, head, genital area, hands and toes</td>
<td>0.1 ml ID at 4 sites on day 0</td>
</tr>
<tr>
<td></td>
<td>3. Multiple deep bites</td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>4. Patient is coming from GIDA* areas, i.e. infrequent transportation to and from ABTC/ABC</td>
<td>0.1 ml ID/IM at 1 site on days 0 and 3</td>
</tr>
<tr>
<td></td>
<td>5. * GIDA – Geographically Isolated and Disadvantaged areas</td>
<td></td>
</tr>
<tr>
<td>Low Risk</td>
<td>Last dose of vaccine was within the previous 3 months <strong>AND</strong></td>
<td>Observe biting animal for 14 days.</td>
</tr>
<tr>
<td></td>
<td>Biting animal is healthy, owned, kept on a leash or can be confined and is available for observation <strong>AND ANY ONE OF THE FF:</strong></td>
<td>If animal remains healthy, withhold booster dose</td>
</tr>
<tr>
<td></td>
<td>1. Biting animal is the same animal that bit the patient previously <strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Biting animal is previously immunized <strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Bite is on the extremities/trunk</td>
<td></td>
</tr>
</tbody>
</table>

E.3. Patients who have previously received complete primary immunization with rabies vaccine have the advantage that booster doses will rapidly induce a large increase in antibody production (a “secondary response”). Therefore, there is no need to give RIG.

E.4. Patients who have not completed the primary immunization as described above shall receive full course including RIG if needed.

f. Management of Rabies Exposures from bites of animals vaccinated against rabies:

f.1. For Category I exposure, PEP is not needed.

f.2. For Category II exposures, the following are recommended:

f.2.1 Immediate washing of the bite wound for ten minutes and application of an antiseptic solution.

f.2.2 No human rabies vaccine shall be provided, provided that ALL of the following conditions are satisfied:
f.2.2.1 Dog/cat is healthy and available for observation for 14 days
f.2.2.2. Dog/cat was vaccinated against rabies for the past 2 years:
   i. Dog/cat shall be at least 1 year 6 months old and has updated vaccination
certificate from a duly licensed veterinarian for the last 2 years
   ii. The last vaccination shall be within the past twelve (12) months, the
   immunization status of the dog/cat shall not be considered updated if
   the animal is not vaccinated on the due date of the next vaccination
f. 2.3. If the biting animal starts to show signs of rabies, immediately give
   vaccine and RIG.
f.2.4. If the biting animal remains to be healthy within 14 days, there is no need to
   administer CCEEV against rabies.

f.3. For Category III exposures, the following are recommended:
f.3.1 Immediate washing of the bite wound for ten minutes and application of
an antiseptic solution.
f.3.2 CCEEV and RIG are immediately administered regardless of the status
of the biting animal.
f.4. PEP shall not be required for bite/s of the following biting animals: rats, mice, guinea
   pigs, hamsters, rabbits, snakes and other reptiles, birds and other avians, insects and
   fish.

Table 10. Clinical Signs of Animal Rabies

<table>
<thead>
<tr>
<th>Prodromal Stage (usually lasts 2-3 days; sometimes only a few hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Changes in attitude/behavior/temperament such as unusual shyness or aggressiveness</td>
</tr>
<tr>
<td>a. Friendly animal becomes aggressive</td>
</tr>
<tr>
<td>b. Solitude</td>
</tr>
<tr>
<td>c. Restlessness</td>
</tr>
<tr>
<td>d. Snapping at imaginary objects</td>
</tr>
<tr>
<td>e. Apprehension</td>
</tr>
<tr>
<td>f. Nervousness</td>
</tr>
<tr>
<td>g. Anxiety</td>
</tr>
<tr>
<td>h. Barking/vocalization at the slightest provocation</td>
</tr>
<tr>
<td>B. Dilated pupils; become myotic in advance state</td>
</tr>
<tr>
<td>C. Mydriasis and/or sluggish palpebral or corneal reflexes</td>
</tr>
<tr>
<td>D. Slight rise in body temperature (slight fever)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Rabies</th>
<th>Paralytic (dumb) stage (develops 2-10 days after clinical signs; usually last 2-4 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furious Stage (usually lasts 1-7 days)</td>
<td>Paralysis</td>
</tr>
</tbody>
</table>
<pre><code>| I. Increased response to auditory and visual stimulation such as |
| • Restlessness |
| • Photophobia |
| • Hyperaesthesia, |
| • Eating unusual objects |
| • Aggression |
| Paralysis may begin at the bite area and progress until entire CNS involvement |
| Following paralysis of the head and neck, the entire body becomes paralyzed |
</code></pre>
<table>
<thead>
<tr>
<th>II. Erratic behavior</th>
<th>Change in tone of vocalization/barking (indicative of laryngeal/pharyngeal paralysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Attacking any live or inanimate objects</td>
<td>• Hypersalivation or frothing; drooling/slobbering of saliva (indicative of laryngeal/pharyngeal paralysis)</td>
</tr>
<tr>
<td>• Biting or snapping</td>
<td>• Dysphagia/difficulty/inability to swallow (indicative of laryngeal/pharyngeal paralysis)</td>
</tr>
<tr>
<td>• Licking or chewing of wound/bite site</td>
<td>• “Jaw drop”/Dropped jaw due to masseter muscle paralysis (suspects foreign body in mouth or esophagus)</td>
</tr>
<tr>
<td>• If caged, biting of their cage</td>
<td>• Pupil dilation or pupil constriction</td>
</tr>
<tr>
<td>• Wandering and roaming</td>
<td>• Protrusion of third eyelid</td>
</tr>
<tr>
<td>• Excitability;</td>
<td>• Ataxia, progressive paralysis and cannibalism (terminal stage)</td>
</tr>
<tr>
<td>• Irritability;</td>
<td>• Coma and/or respiratory paralysis resulting in death within 2-4 days</td>
</tr>
<tr>
<td>• Viciousness</td>
<td></td>
</tr>
</tbody>
</table>

III. Self-mutilation

IV. Muscular in-coordination and seizures

V. Disorientation
• Roams and bites inanimate object and also other animals including man

### D. Pre-exposure Prophylaxis

a. Benefits
- The need for passive immunization product (RIG) is eliminated
- PET vaccine regimen is reduced from five to two doses
- Protection against rabies is possible if PET is delayed
- Protection against inadvertent exposure to rabies is possible
- The cost of PEP is reduced

b. Target population
- Personnel in rabies diagnostic laboratories
- Veterinarians and veterinary students
- Animal handlers
- Health care workers directly involved in care of rabies patients
- Individuals directly involved in rabies control
- Field workers
- It is recommended that children 2-10 yrs old also be immunized because of the increased risk and severity of animal bites in this age group
c. Regimen:

**Table 11. Pre-exposure Prophylaxis Schedule**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>PVRV</th>
<th>PCECV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 7</td>
</tr>
<tr>
<td>Intradermal (2 doses)</td>
<td>0.1 ml</td>
<td>0.1 ml</td>
</tr>
<tr>
<td>Intramuscular*</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
</tr>
</tbody>
</table>

* Immunocompromised individuals should receive the full intramuscular regimen (Day 0, 7 and 21/28).
** For Immunocompetent individuals given WHO Pre-qualified CCEEV, Day 21/28 is not given.
For Immunocompetent individuals given non-WHO prequalified CCEEV, Day 21/28 is given

d. Routine booster schedule for individual given Pre- Exposure Prophylaxis: (Table 12)

Not all individuals who have completed the PrEP shall receive routine booster doses of anti-rabies vaccine. Only high risk individuals whose exposures may not be known are recommended to have routine booster doses.

**Table 12. Routine booster Schedule for individuals given Pre- Exposure Prophylaxis (PreP)**

<table>
<thead>
<tr>
<th>Type of Risk</th>
<th>Population at Risk</th>
<th>Recommended Booster Schedule (Without definite exposure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk (exposures may not be known)</td>
<td>1. Health workers handling rabies cases</td>
<td>- 1 Booster dose 1 year after primary immunization:</td>
</tr>
<tr>
<td></td>
<td>2. Workers in rabies laboratories</td>
<td>a. One (1 site) 0.1 ml ID dose of PVRV or PCEC on DO; OR</td>
</tr>
<tr>
<td></td>
<td>3. Veterinarians,</td>
<td>b. One (1 site) Vial of 0.5 ml PVRV or 1.0 ml PCEC given intramuscularly on DO</td>
</tr>
<tr>
<td></td>
<td>4. Veterinary students,</td>
<td>- Thereafter, 1 booster, if Ab titers fall below 0.5 IU/ml</td>
</tr>
<tr>
<td></td>
<td>5. Animal handlers (dog trainers, workers in pet shops, zoos, etc.)</td>
<td>OR</td>
</tr>
<tr>
<td>Low Risk (exposures are known)</td>
<td>General Population</td>
<td>- In the absence of serologic testing, 1 booster dose every 5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>primary immunization after immunization</td>
</tr>
</tbody>
</table>
E. Management of the Biting Animal

1. The biting animal shall be observed for 14 days. Adequate animal care shall be provided during the observation period.

2. It is advisable for patients to consult a veterinarian, whenever possible, regarding biting animal management especially when any of the following is observed:
   a. sudden change of behavior (from mild to vicious temperament or vice versa)
   b. characteristic hoarse howl
   c. watchful, apprehensive expression of the eyes, staring, blank gaze
   d. drooling of saliva
   e. paralysis or uncoordinated gait of hind legs
   f. marked restlessness, pacing in cage
   g. if at large runs aimlessly, biting anything in its way
   h. deprived appetite, self-mutilation
   i. in some cases, lies quiescent, biting when provoked
   j. snaps at imaginary objects
   k. paralysis of lower jaw and tongue; inability to drink
   l. sudden death without associated S/Sx

3. PEP utilizing non-WHO prequalified vaccine shall be discontinued if the biting animal remains healthy after the 14-day observation period. If the animal dies or gets sick, the head shall be submitted to the nearest rabies diagnostic laboratory for testing.

F. Dispensing of Anti-Rabies Immunizing Agent

1. Patients needing PEP shall be referred to the nearest Animal Bite Treatment Center/Animal Bite Clinic where anti-rabies immunizing agents (vaccines and RIG) are administered.

2. The following procedures shall be observed when assessing animal bite patients and dispensing anti-rabies immunizing agents:
   a. Assess the victim thoroughly and record in the Municipal/City/Hospital Rabies Surveillance Form (Facility-based form).
   b. Decide whether or not to initiate treatment using the Revised Guidelines on the Management of Animal Bite Patients as reference.
   c. If the situation warrants immunization (Category II and Category III), the patient shall be given the intradermal regimen. The other approved regimens may be used if the ID regimen is not feasible
   d. If indicated, the patient shall be provided the required dose of passive immunization products/RIG, if available, preferably ERIG or F(ab')2.
   e. Explain your decision to the patient with particular emphasis on adherence to treatment schedules, if immunization is indicated.
f. Observe courtesy and tactfulness when dealing with patients particularly among individuals who need not be immunized.
g. Give advice on the practice of Responsible Pet Ownership.

G. Priorities for Dispensing Vaccines
The following shall be the program’s order of priority for dispensing vaccines:
a. Patients bitten by animals found to be positive by IFAT or for “Negri bodies” regardless of type of bite exposure
b. Patients with Category III exposure
c. Patients bitten by animals that are not available for observation (stray/slaughtered)
d. Individuals exposed to human rabies patients through bite/non-bite exposure as defined in table 1.
e. Patients with Category II exposure

H. Injection Safety:
A safe injection is defined by the World Health Organization as an injection that:
- Does not harm the recipient
- Does not expose the health staff to any avoidable risks
- Does not result in waste that is dangerous to the community.

1. Injection Equipment
   b. Auto-Disable (AD) Syringes—are disposable injection devices that are especially made to prevent re-use and are therefore less likely than standard disposable syringes to cause person-to-person transmission of blood-borne diseases.

   The program recommends that health workers shall use AD syringe in their respective ABTC.

c. Conventional Syringes—are plastic syringes with steel needles that are provided usually by the manufacturer in sterile package. The needle may either be fixed to the syringe when it is produced or attached by the health staff just before use.

2. Management of Sharp Wastes
   Used syringes and needles shall never be dumped in open areas where people might pick them up, step on them, or come in contact with them in any way.

   The need to better manage used or contaminated sharps shall be through the use of safety boxes or sharp containers. These are puncture-resistant containers where used syringes and needles can be immediately and temporarily stored after use until its final disposal.

3. Waste Disposal
   Collector boxes filled with used syringes and needles shall be immediately brought to its final disposal. The program recommends the following methods of disposal:
   - Use of septic vault
• Pit burial; and
• Waste treatment and final disposal to landfill

I. Roles and Responsibilities

1. Central Office
   The Disease Prevention and Control Bureau shall be responsible for procurement, allocation and distribution of vaccines and RIG and shall augment vaccine requirements for low-income municipalities with high incidence of rabies. All DOH Regional Offices shall be given allocation every quarter subject to availability of the immunological products.

2. DOH Regional Office
   The Regional Office, through the Director and the Rabies Control Program Coordinator shall be responsible for distribution of vaccines to the Provincial/City Health Offices.

3. Local Government Units (LGUs)
   The LGUs shall be encouraged to enact and strictly enforce ordinance relevant to rabies control. The Provincial Rabies Control Coordinators shall distribute the augmented vaccines of the Department of Health to the established Animal Bite Treatment Centers where human anti-rabies immunizing agents (vaccines and RIG) are administered. The LGUs shall encourage to allocate funds for its procurement.

VII. TRANSITORY PROVISION

Procurement of NON-WHO PREQUALIFIED CCEEV for government agencies shall cease when WHO pre-qualified vaccines become available and supplies become stable in the market.

VIII. REPEALING CLAUSE

Administrative Order No. 2014-0012 entitled “New Guidelines on the Management of Rabies Exposures” and all other issuances inconsistent or contrary to the provisions of this Order are hereby repealed or modified.

IX. EFFECTIVITY

This Order shall take effect immediately.

FRANCISCO T. DUQUE, M.D., M.Sc.
Secretary of Health